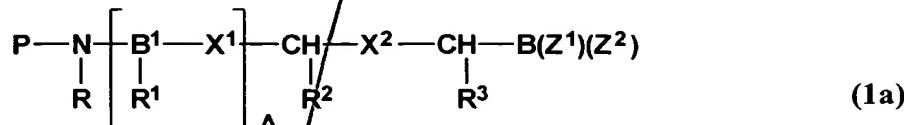


What Is Claimed Is:

1. A compound having the formula:



and pharmaceutically acceptable salts thereof;

5 wherein

P is $R^7-C(O)-$ or R^7-SO_2- , where R^7 is one of aryl, aralkyl, heteroaryl or heteroarylalkyl, the ring portion of any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl;

10 B^1 , at each occurrence, is independently one of N or CH;

15 X^1 , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B^1 is N, then the X^1 attached to said B^1 is $-C(O)-NH-$;

20 X^2 is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

R is hydrogen or alkyl, or R forms together with the adjacent R^1 , or when A is zero, forms together with the adjacent R^2 , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

25 R^1 , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R² is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

5 R³ is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

10 R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z¹ and Z² are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom

15 ~~or heteroatoms which can be N, S, or O, and~~

A is 0, 1, or 2.

2. The compound of claim 1, wherein:

A is zero;

X is -C(O)-NH-;

20 R is hydrogen or C₁₋₈alkyl; and

R₃ is C₁₋₆alkyl.

3. The compound of claim 2, wherein R₃ is C₄alkyl.

4. The compound of claim 1, wherein:

25 P is R⁷-C(O)- or R⁷-SO₂-~~-,~~, where R⁷ is one of quinolinyl, quinoxalinyl, pyridyl, pyrazinyl, furanyl or pyrrolyl, or when P is R⁷-C(O)-, R⁷ can also be N-morpholinyl.

A
X 5. The compound of claim ~~X~~, wherein P is one of quinolinecarbonyl, pyridinecarbonyl, quinolinesulfonyl, quinoxalinecarbonyl, quinoxalinesulfonyl, pyrazinecarbonyl, pyrazinesulfonyl, furancarbonyl, furansulfonyl or N-morpholinylcarbonyl.

Six 5 6. The compound of claim 5, wherein P is one of 8-quinolinecarbonyl, 8-quinolinesulfonyl, 2-quinoxalinecarbonyl, 2-quinoxalinesulfonyl, 2-pyrazinecarbonyl, 2-pyrazinesulfonyl, 3-furancarbonyl, 3-furansulfonyl or N-morpholinecarbonyl.

10 7. The compound of claim 1, wherein A is 0.

8. The compound of claim 1, wherein B¹, at each occurrence, is CH.

9. The compound of claim 8, wherein X¹, at each occurrence, is -C(O)-NH-.

10. The compound of claim 9, wherein X² is -C(O)-NH-.

K 5 11. The compound of claim ~~X~~, wherein R is hydrogen or C₁₋₈ alkyl.

15 12. The compound of claim 1, wherein: R¹, at each occurrence, and R² and R³ are each independently one of hydrogen, C₁₋₈ alkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, a 5-, 6-, 9- or 10- membered heteroaryl group, or -CH₂-R⁵;

20 R⁵, in each instance, is one of C₆₋₁₀ aryl, C₆₋₁₀ ar(C₁₋₆)alkyl, C₁₋₆ alk(C₆₋₁₀)aryl, C₃₋₁₀ cycloalkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio or a 5-, 6-, 9- or 10- membered heteroaryl group;

where the ring portion of any of said aryl, aralkyl, alkaryl or 5-, 6-, 9- or 10- membered heteroaryl groups of R¹, R², R³ and R⁵ can be optionally

substituted by one or two substituents independently selected from the group consisting of C₁₋₆alkyl, C₃₋₈cycloalkyl, C₁₋₆alkyl(C₃₋₈)cycloalkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, cyano, amino, C₁₋₆alkylamino, di(C₁₋₆)alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C₁₋₆)alkoxy, trifluoromethyl, halogen, C₁₋₆alkoxy, C₆₋₁₀aryl, C₆₋₁₀aryl(C₁₋₆)alkyl, C₆₋₁₀aryl(C₁₋₆)alkoxy, hydroxy, C₁₋₆alkylthio, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₆₋₁₀arylthio, C₆₋₁₀arylsulfinyl, C₆₋₁₀arylsulfonyl, C₆₋₁₀aryl, C₁₋₆alkyl(C₆₋₁₀)aryl, and halo(C₆₋₁₀)aryl.

5

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13. The compound of claim 1, wherein R₃ is C₁₋₁₂alkyl.

8
14. The compound of claim 1, wherein R₃ is C₁₋₆alkyl.

9
15. The compound of claim 1, wherein R₃ is C₄alkyl.

10
16. The compound of claim 1, wherein R³ is isobutyl.

A

A

R

R

15

17. The compound of claim 1, wherein R² is one of isobutyl, 1-naphthylmethyl, 2-naphthylmethyl, 3-pyridylmethyl, 2-pyridylmethyl, 6-quinolinylmethyl, 3-indolylmethyl, benzyl, 4-fluorobenzyl, 4-hydroxybenzyl, 4-(2'-pyridylmethoxy)benzyl, 4-(benzyloxy)benzyl, benzylnaphthylmethyl or phenethyl.

18. The compound of claim 1, wherein Z¹ and Z² are independently one of C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy.

19. The compound of claim 18, wherein Z¹ and Z² are both hydroxy.

20

20. The compound of claim 1, wherein together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting

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of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

(15) 21. The compound of claim 1, wherein:

P is one of quinolinecarbonyl, pyridinecarbonyl, quinolinesulfonyl, quinoxalinecarbonyl, quinoxalinesulfonyl, pyrazinecarbonyl, pyrazinesulfonyl, furancarbonyl, furansulfonyl or N-morpholinylcarbonyl;

A is zero;

X² is -C(O)-NH-;

R is hydrogen or C₁₋₈ alkyl;

R² and R³ are each independently one of hydrogen, C₁₋₈alkyl, C₃₋₁₀cycloalkyl, C₆₋₁₀aryl, C₆₋₁₀ar(C₁₋₆)alkyl, pyridylmethyl, or quinolinylmethyl; and

Z¹ and Z² are both hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

5b/1 22. The compound of claim 1, wherein:

P is one of 8-quinolinecarbonyl, 8-quinolinesulfonyl, 2-quinoxalinecarbonyl, 2-quinoxalinesulfonyl, 2-pyrazinecarbonyl, 2-pyrazinesulfonyl, 3-pyridinecarbonyl, 3-pyridinesulfonyl, 3-furancarbonyl, 3-furansulfonyl or N-morpholinecarbonyl;

A is zero;

X² is -C(O)-NH-;

R is hydrogen or C₁₋₈ alkyl;

R³ is isobutyl;

R² is one of isobutyl, 1-naphthylmethyl, 2-naphthylmethyl, 3-pyridylmethyl, 2-pyridylmethyl 6-quinolinylmethyl, 3-indolylmethyl, benzyl,

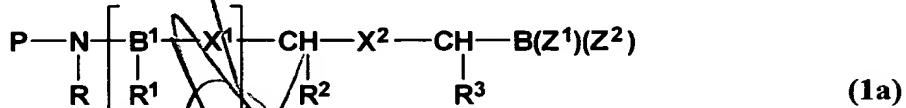
4-fluorobenzyl, 4-hydroxybenzyl, 4-(2'-pyridylmethoxy)benzyl,
4-(benzyloxy)benzyl, benzylnaphthylmethyl or phenethyl; and

5 ~~Z¹ and Z² are independently one of hydroxy, C₁₋₆alkoxy, C₆₋₁₀aryloxy, or
together Z¹ and Z² form a moiety derived from a dihydroxy compound selected
from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene
glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol,
glycerol or diethanolamine.~~

12 23. The compound of claim 1, wherein said compound is one of:
~~go /~~
N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid,
N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-(O-benzyl)-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-[O-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic
acid;
or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

20 24. The compound of claim 23, wherein said compound is
N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid, or an isostere,
pharmaceutically acceptable salt or boronate ester thereof.

25. A compound having the formula:



wherein

P is hydrogen or an amino-group-protecting moiety;

B¹, at each occurrence, is independently one of N or CH;

X¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-,
5 -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-,
-C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided
that when B¹ is N, then the X¹ attached to said B¹ is -C(O)-NH-;

X² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-,
-C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

10 R is hydrogen or alkyl, or R forms together with the adjacent R¹, or when
A is zero, forms together with the adjacent R², a nitrogen-containing mono-, bi-
or tri-cyclic, saturated or partially saturated ring system having 4-14 ring
members, that can be optionally substituted by one or two of keto, hydroxy, aryl,
alkoxy or aryloxy;

15 R¹ at each occurrence, R² and R³ are each independently one of hydrogen,
alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or
aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl,
aralkyl, alkaryl or heterocycle can be optionally substituted;

20 R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a
5-10 membered saturated, partially unsaturated or aromatic
heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl,
where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

25 provided that at least one R¹, R² or R³ is naphthylmethyl,
pyridylmethyl or quinolinylmethyl;

Z¹ and Z² are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or
together Z¹ and Z² form a moiety derived from a dihydroxy compound having at
least two hydroxy groups separated by at least two connecting atoms in a chain
or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom
30 or heteroatoms which can be N, S, or O; and

or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A is 0, 1, or 2;

provided that the compound is other than isovaleryl-phenylalanine-norvaline-[(naphthylmethyl), (4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)]methylamide or (3-t-butylsulfonyl)propionyl-norvaline-(1-naphthyl, dihydroxyboryl)methylamide.

26. The compound of claim 25, wherein P is $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also be saturated or partially saturated heterocycle.

27. The compound of claim 25, wherein P is $R^7-C(O)-$ or R^7-SO_2- ; and

R^7 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, 5- to 10-membered heteroaryl or 5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

28. The compound of claim 25, wherein B^1 is CH, and X^1 and X^2 are each $-C(O)-NH-$.

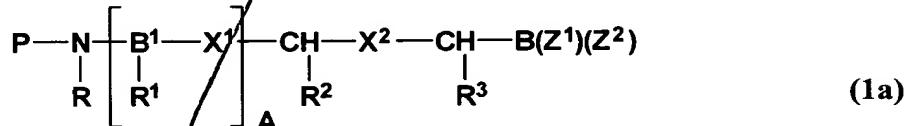
29. The compound of claim 25, wherein R^1 and R^2 are independently selected from the group consisting of alkyl and $-CH_2-R^5$, where R^5 is one of C_{6-10} aryl, C_{1-10} alk(C_{6-10})aryl, C_{3-10} cycloalkyl, or a 5-, 6-, 9- or 10-membered heterocycle.

30. The compound of claim 25, wherein A is zero.

31. The compound of claim 25, wherein R² is quinolinylmethyl.

32. The compound of claim 25, wherein said compound is one of:
N-(4-morpholine)carbonyl- β -(1-naphthyl)-L-alanine-L-leucine boronic acid, or
N-(8-quinoline)sulfonyl- β -(1-naphthyl)-L-alanine-L-leucine boronic acid;
or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

33. A compound having the formula:



and pharmaceutically acceptable salts thereof;

wherein

10 P is hydrogen or an amino-group-protecting moiety;

B^1 , at each occurrence, is independently one of N or CH;

X^1 , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B^1 is N , then the X^1 attached to said B^1 is $-C(O)-NH-$;

15 that when B¹ is N, then the X¹ attached to said B¹ is -C(O)-NH-;

X^2 is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$,
 $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

R forms together with the adjacent R¹, or when A is zero, forms together with the adjacent R², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, and one or two optional substituents selected from the group consisting of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy and aryloxy;

when A is 2, the R¹ that is not adjacent to N-R is one of hydrogen, alkyl, cycloalkyl, aryl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵;

when A is 1 or 2, R² is one of hydrogen, alkyl, cycloalkyl, aryl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵;

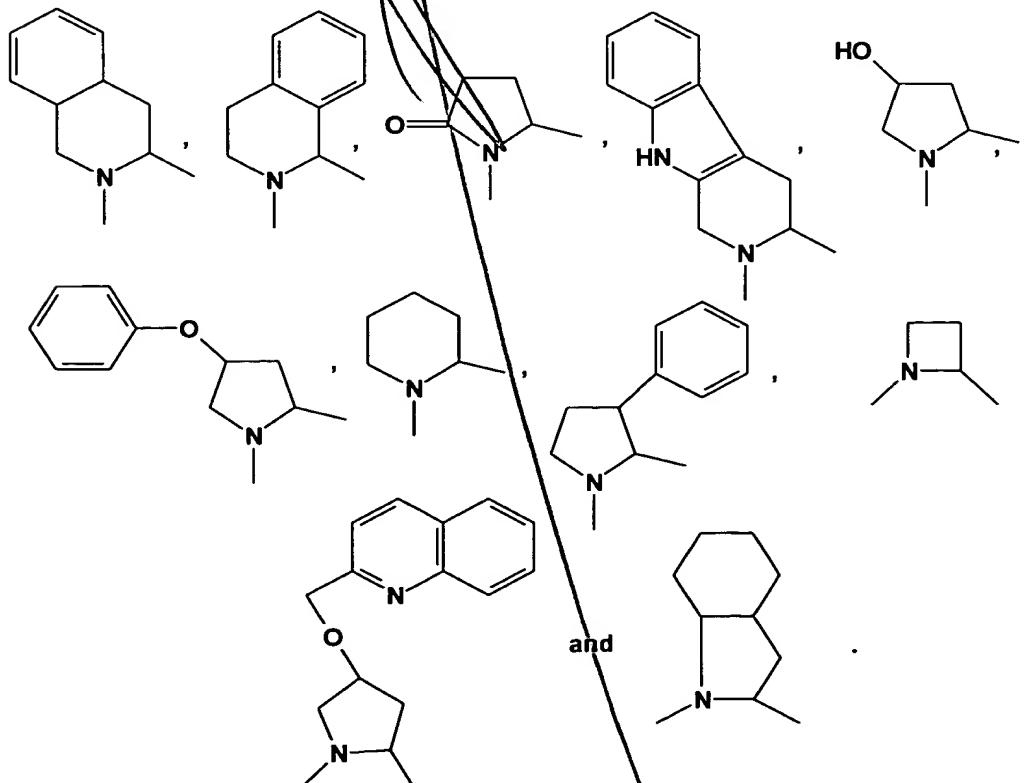
R^3 is one of hydrogen, alkyl, cycloalkyl, aryl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^5$;

5 R⁵, in each instance, is independently one of aryl, aralkyl, alkaryl, cycloalkyl, a 5- to 10-membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl;

Z^1 and Z^2 are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z^1 and Z^2 form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A is 0, 1, or 2.

34. The compound of claim 33, wherein the nitrogen-containing ring system is selected from the group consisting of:



35. The compound of claim 33, wherein P is $R^7-C(O)-$, R^7-SO_2- ,
 $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, any
of which can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also
be saturated or partially saturated heterocycle.

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36. The compound of claim 35, wherein P is $R^7-C(O)-$ or R^7-SO_2- ;
and

R^7 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, 5- to 10-membered heteroaryl or
5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally
substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

10

37. The compound of claim 33, wherein B^1 is CH, and X^1 and X^2 are
each $-C(O)-NH-$.

38. The compound of claim 33, wherein R^1 and R^2 are independently
selected from the group consisting of alkyl and $-CH_2-R^5$, where

15

R^5 , in each instance, is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, C_{1-6}
alk(C_{6-10})aryl, C_{3-10} cycloalkyl, C_{1-8} alkoxy, C_{1-8} alkylthio or a 5-, 6-, 9- or 10-
membered heteroaryl group, where the ring portion of any of said C_{6-10} aryl, C_{6-10}
ar(C_{1-6})alkyl, C_{1-6} alk(C_{6-10})aryl, or 5-, 6-, 9- or 10- membered heteroaryl can be
optionally substituted by one or two substituents independently selected from the
group consisting of C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl(C_{3-8})cycloalkyl, C_{2-8}
alkenyl, C_{2-8} alkynyl, cyano, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino,
benzylamino, dibenzylamino, nitro, carboxy, carbo(C_{1-6})alkoxy, trifluoromethyl,
halogen, C_{1-6} alkoxy, C_{6-10} aryl, C_{6-10} aryl(C_{1-6})alkyl, C_{6-10} aryl(C_{1-6})alkoxy,
hydroxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{6-10} arylthio, C_{6-10}
arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} aryl, C_{1-6} alkyl(C_{6-10})aryl and halo(C_{6-10})aryl.

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39. The compound of claim 33, wherein A is zero.

40. The compound of claim 33, wherein P is hydrogen.

41. The compound of claim 33, wherein:

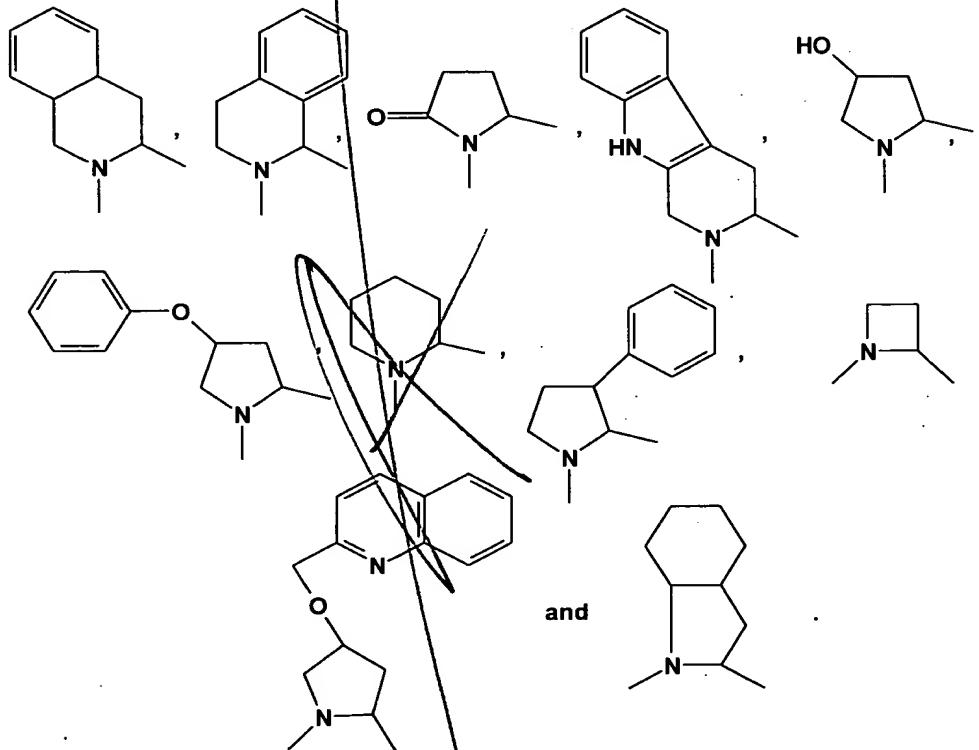
A is zero;

P is hydrogen;

X^2 is $-C(O)-NH-$

5

R forms together with the adjacent R², a nitrogen-containing ring system selected from the group consisting of:



R³ is C₁₋₆alkyl; and

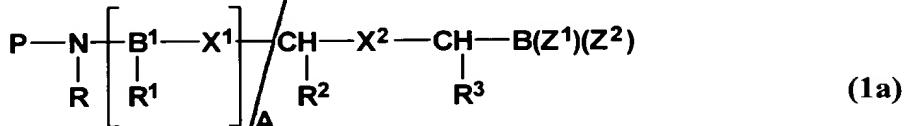
10

Z^1 and Z^2 are both hydroxy, C_1-C_6 alkoxy, or C_{6-10} aryloxy, or together Z^1 and Z^2 form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene

glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

5 42. The compound of claim 33, wherein said compound is L-proline-L-leucine boronic acid, or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

10 43. A compound having the formula:



15 and pharmaceutically acceptable salts thereof;
wherein

P is hydrogen or an amino-group-protecting moiety;

B¹, at each occurrence, is independently one of N or CH;

X¹, at each occurrence, is independently one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-, -CH(CH₃)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-, provided that when B¹ is N, then the X¹ attached to said B¹ is -C(O)-NH-;

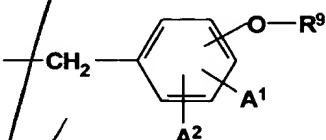
X² is one of -C(O)-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

20 R is hydrogen or alkyl, or R forms together with the adjacent R¹, or when A is zero, forms together with the adjacent R², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, and one or two optional substituents selected from the group consisting of keto, hydroxy, aryl, alkoxy and aryloxy;

R¹ at each occurrence, R² and R³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or

aromatic heterocycle or $-\text{CH}_2-\text{R}^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

5 R^5 , in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-\text{W}-\text{R}^6$, where W is a chalcogen and R^6 is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,
provided that at least one R^1 , R^2 or R^3 is



10 where R^9 is one of hydrogen, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or heteroarylalkyl; wherein the alkyl is optionally substituted with one of C_{1-6} alkyl, halogen monohalo (C_{1-6})alkyl and trifluoromethyl; and wherein said cycloalkyl, aryl, aralkyl, heteroaryl and heteroarylalkyl groups can be optionally substituted with one or two of C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkyl(C_{3-8})cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, cyano, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C_{1-6})alkoxy, trifluoromethyl, halogen, C_{1-6} alkoxy, C_{6-10} aryl, C_{6-10} aryl(C_{1-6})alkyl, C_{6-10} aryl(C_{1-6})alkoxy, hydroxy, C_{1-6} alkylthio, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{6-10} arylthio, C_{6-10} arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} aryl, C_{1-6} alkyl(C_{6-10})aryl, and halo(C_{6-10})aryl;

15 A^1 and A^2 are independently one of hydrogen, halogen, C_{1-6} alkyl, monohalo(C_{1-6})alkyl, or trifluoromethyl;

20 Z^1 and Z^2 are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z^1 and Z^2 form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain

or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A is 0, 1, or 2.

44. The compound of claim 43, wherein P is $R^7-C(O)-$, R^7-SO_2- ,
5 $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, and

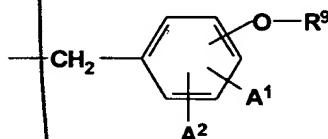
R^7 is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, then R^7 can also be saturated or partially saturated heterocycle.

45. The compound of claim 43, wherein P is $R^7-C(O)-$ or R^7-SO_2- ;
10 and

R^7 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, 5- to 10-membered heteroaryl or 5- to 10-membered heteroaryl(C_{1-6})alkyl, any of which can be optionally substituted, or when P is $R^7-C(O)-$, R^7 can also be N-morpholinyl.

46. The compound of claim 43, wherein X^1 and X^2 are each
15 $-C(O)-NH-$.

47. The compound of claim 43, wherein one of R^1 , R^2 or R^3 is



where

A¹ and A² are independently one of hydrogen, C_{1-6} alkyl, halogen, monohalo (C_{1-6}) alkyl or trifluoromethyl;

20 R⁹ is one of C_{1-8} alkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, a 5- to 10-membered heteroaryl or a 5- to 10-membered heteroaryl(C_{1-6})alkyl;

and the remaining R¹, R² and R³ are independently selected from the group consisting of alkyl and —CH₂—R⁵, where

R⁵, in each instance, is one of C₆₋₁₀ aryl, C₆₋₁₀ ar(C₁₋₆)alkyl, C₁₋₆ alk(C₆₋₁₀)aryl, C₃₋₁₀ cycloalkyl, C₁₋₈ alkoxy, C₁₋₈ alkylthio or a 5-, 6-, 9- or 10-membered heteroaryl group, where the ring portion of any of said C₆₋₁₀ aryl, C₆₋₁₀ ar(C₁₋₆)alkyl, C₁₋₆ alk(C₆₋₁₀)aryl, or 5-, 6-, 9- or 10-membered heteroaryl can be optionally substituted by one or two substituents independently selected from the group consisting of C₁₋₆ alkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkyl(C₃₋₈)cycloalkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, cyano, amino, C₁₋₆ alkylamino, di(C₁₋₆)alkylamino, benzylamino, dibenzylamino, nitro, carboxy, carbo(C₁₋₆)alkoxy, trifluoromethyl, halogen, C₁₋₆ alkoxy, C₆₋₁₀ aryl, C₆₋₁₀ aryl(C₁₋₆)alkyl, C₆₋₁₀ aryl(C₁₋₆)alkoxy, hydroxy, C₁₋₆ alkylthio, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, C₆₋₁₀ arylthio, C₆₋₁₀ arylsulfinyl, C₆₋₁₀ arylsulfonyl, C₆₋₁₀ aryl, C₁₋₆ alkyl(C₆₋₁₀)aryl and halo(C₆₋₁₀)aryl.

48. The compound of claim 43, wherein A is zero.

49. The compound of claim 43, wherein:

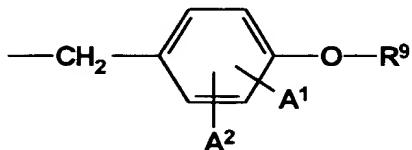
A is zero;

P is one of R⁷—C(O)—, R⁷—SO₂—, R⁷—NH—C(O)— or R⁷—O—C(O)—;

R⁷ is one of quinolinyl, quinoxaliny, pyridyl, pyrazinyl, furanyl or pyrrolyl, or when P is R⁷—C(O)—, R⁷ can also be N-morpholinyl;

X² is —C(O)–NH—;

R² is:



where

A¹ and A² are independently one of hydrogen, C₁₋₆ alkyl, halogen, monohalo (C₁₋₆) alkyl or trifluoromethyl;

R⁹ is one of hydrogen, C₁₋₈alkyl, phenyl, benzyl, phenethyl or pyridylmethyl;

R³ is C₁₋₆alkyl; and

Z¹ and Z² are both hydroxy, C₁₋₆alkoxy, or C₆₋₁₀aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound selected from the group consisting of pinacol, perfluoropinacol, pinanediol, ethylene glycol, diethylene glycol, 1,2-cyclohexanediol, 1,3-propanediol, 2,3-butanediol, glycerol or diethanolamine.

50. The compound of claim 43, wherein said compound is one of:

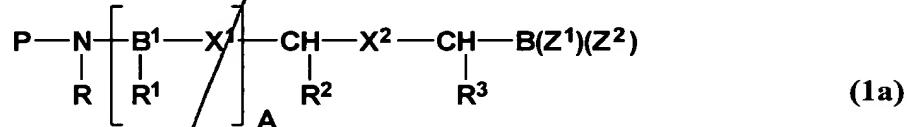
10 N-(4-morpholine)carbonyl-(O-benzyl)-L-tyrosine-L-leucine boronic acid,

N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid, or

N-(4-morpholine)carbonyl-[O-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid; or

isosteres, pharmaceutically acceptable salts or boronate esters thereof.

15 51. A compound having the formula:



and pharmaceutically acceptable salts thereof;

wherein

A is zero;

20 P is hydrogen or an amino-group-protecting moiety;

X² is one of -C(O)-NH-, -CH₂-NH-, -CH(OH)-CH₂-, -CH(OH)-CH(OH)-, -CH(OH)-CH₂-NH-, -CH=CH-, -C(O)-CH₂-, -SO₂-NH-, -SO₂-CH₂- or -CH(OH)-CH₂-C(O)-NH-;

25 R is hydrogen or alkyl, or R forms together with the adjacent R², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring

system having 4-14 ring members, where said ring system can be optionally substituted by one or two of keto, hydroxy, aryl, alkoxy or aryloxy;

5 R² and R³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

10 R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted; and

15 Z¹ and Z² are independently one of alkyl, hydroxy, alkoxy, or aryloxy, or together Z¹ and Z² form a moiety derived from a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O;

provided that P is not C₁₋₆ alkoxycarbonyl, C₁₋₄ alkylcarbonyl or phenyl(C₁₋₃)alkyl.

20 52. The compound of claim 51, wherein P is R⁷-C(O)-, R⁷-SO₂-, R⁷-NH-C(O)- or R⁷-O-C(O)-, and

R⁷ is one of alkyl, aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl, where the ring portion of any of said aryl, alkaryl, aralkyl, heteroaryl or heteroarylalkyl can be optionally substituted, or when P is R⁷-C(O)-, then R⁷ can also be a saturated or partially unsaturated heterocycle.

25 53. The compound of claim 51, wherein P is R⁷-C(O)- or R⁷-SO₂-, and

R⁷ is one of C₆₋₁₀ aryl, C₆₋₁₀ ar(C₁₋₆)alkyl, a 5- to 10-membered heteroaryl or a 5- to 10-membered heteroaryl(C₁₋₆)alkyl, any of which can be optionally substituted, or when P is R⁷—C(O)—, R⁷ can also be N-morpholinyl.

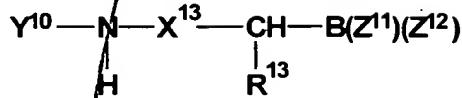
5 54. The compound of claim 51, wherein B¹ is CH, and X¹ and X² are each —C(O)—NH—.

55. The compound of claim 51, wherein R² and R³ are independently selected from the group consisting of C₁₋₈ alkyl and —CH₂—R⁵, where R⁵ is one of C₆₋₁₀ aryl, C₁₋₆ alk(C₆₋₁₀)aryl, C₆₋₁₀ ar(C₁₋₆)alkyl, C₃₋₈ cycloalkyl, or a 5-, 6-, 9- or 10-membered heterocycle.

10 56. The compound of claim 51, which is *N*-(3-phenylpropionyl)-L-phenylalanine-L-leucine boronic acid, or isosteres, pharmaceutically acceptable salts or boronate esters thereof.

15 57. The compound of claim 51, wherein said compound is one of:
N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid,
N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,
20 *N*-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid,
N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid, or
N-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid; or
isosteres, pharmaceutically acceptable salts or boronate esters thereof.

58. A compound having the formula:



(2a)

and pharmaceutically acceptable salts thereof;

wherein

5 Y is one of $R^8-C(O)-$, R^8-SO_2- , $R^8-NH-C(O)-$ or $R^8-O-C(O)-$, where R^8 is one of alkyl, aryl, alkaryl, aralkyl, any of which can be optionally substituted, or when Y is $R^8-C(O)-$ or R^8-SO_2- , then R^8 can also be an optionally substituted 5-10 membered, saturated, partially unsaturated or aromatic heterocycle;

10 X³ is a covalent bond or $-C(O)-CH_2-$;

15 R³ is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

20 R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-W-R^6$, where W is a chalcogen and R⁶ is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted; and

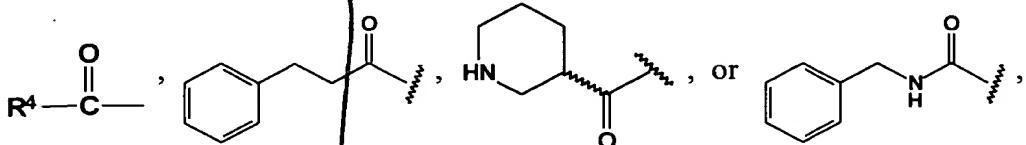
25 Z¹ and Z² are independently alkyl, hydroxy, alkoxy, aryloxy, or together form a moiety derived from dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O;

provided that when Y is $R^8-C(O)-$, R⁸ is other than phenyl, benzyl or C₁₋₃ alkyl.

25 59. The compound of claim 58, wherein P is $R^8-C(O)-$ or R^8-SO_2- ; and

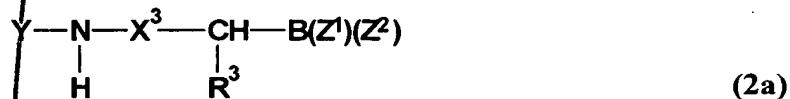
R^8 is one of C_{6-10} aryl, C_{6-10} ar(C_{1-6})alkyl, or a 5-10 membered heteroaryl, any of which can be optionally substituted, or when P is $R^8-C(O)-$, R^8 can also be N-morpholinyl.

60. The compound according to claim 58, wherein Y is one of



where R^4 is C_{6-12} alkyl.

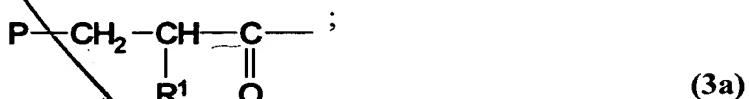
61. A compound having the formula:



and pharmaceutically acceptable salts thereof;

where

Y is



P is one of $R^7-C(O)-$, R^7-SO_2- , $R^7-NH-C(O)-$ or $R^7-O-C(O)-$, where

15 R^7 is one of alkyl, aryl, alkaryl, aralkyl, any of which can be optionally substituted, or when Y is $R^7-C(O)-$ or R^7-SO_2- , R^7 can also be an optionally substituted 5-10 membered saturated, partially unsaturated or aromatic heterocycle;

X^3 is a covalent bond or $-C(O)-CH_2-$;

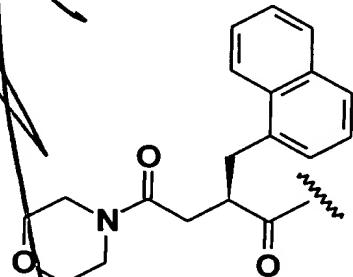
20 R^1 , at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^5$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R³ is one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

5 R⁵, in each instance, is one of aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -W-R⁶, where W is a chalcogen and R⁶ is alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted; and

10 Z¹ and Z² are independently alkyl, hydroxy, alkoxy, aryloxy, or together form a moiety derived from dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O.

62. The compound of claim 61, wherein Y is:



15 63. A pharmaceutical composition, comprising a compound of claims 1, 25, 33, 43, 51, 58 or 61, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

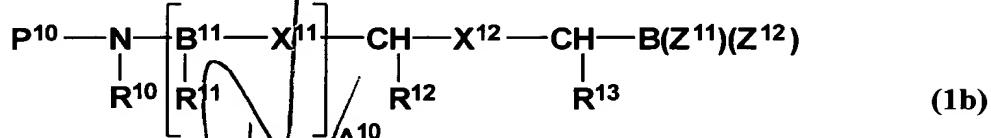
20 64. A pharmaceutical composition, comprising a compound of claims 22, 28, 41, 49, 55, 60 and 62, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

65. A pharmaceutical composition, comprising a compound of claims 23, 32, 42, 50, 56 and 57 or an isostere, pharmaceutically acceptable salt or boronate ester thereof, and a pharmaceutically acceptable carrier or diluent.

5 66. The pharmaceutical composition of claim 65, wherein said compound is present in an amount effective to inhibit the proteasome function in a mammal.

67. A method of inhibiting the growth of a cancer cell, comprising contacting a cell in need of such inhibiting with an effective growth-inhibiting amount of a compound of claims 1, 25, 33, 43, 51, 58 or 61.

10 68. A method for reducing the rate of muscle protein degradation in a cell comprising contacting a cell in need of said reducing with an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

15 wherein

P^{10} is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

20 X^{11} , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B^{11} is N, then X^{11} is $-C(O)-NH-$;

X^{12} is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

5 R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

10 R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

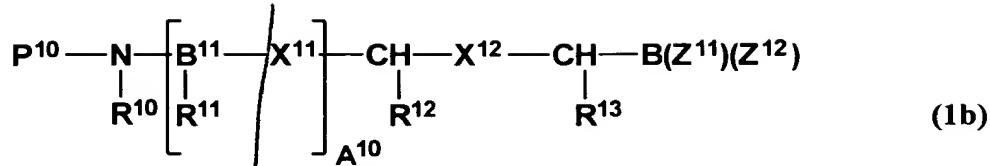
15 R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

20 where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or -chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

25 Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and Z¹² together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A¹⁰ is 0, 1, or 2

69. A method for reducing the activity of NF-κB in a cell, comprising contacting a cell in need of said reducing with an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

5 B¹¹ is independently one of N or CH;

X¹¹, at each occurrence, is independently one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}_2-\text{NH}-$,
 $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$, $-\text{CH}(\text{OH})-\text{CH}_2-\text{NH}-$, $-\text{CH}=\text{CH}-$,
 $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$, provided
that when B¹¹ is N, then X¹¹ is $-\text{C}(\text{O})-\text{NH}$;

10 X¹² is one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$,
 $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$;

15 R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or
when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing
mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14
ring members, that can be optionally substituted by one or two of keto, hydroxy,
alkyl, aryl, aralkyl, alkoxy or aryloxy;

20 R¹¹, at each occurrence, is independently one of hydrogen, alkyl,
cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic
heterocycle or $-\text{CH}_2-\text{R}¹⁵$, where the ring portion of any of said aryl, aralkyl,
alkaryl or heterocycle can be optionally substituted;

25 R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl,
aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or
 $-\text{CH}_2-\text{R}¹⁵$, where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

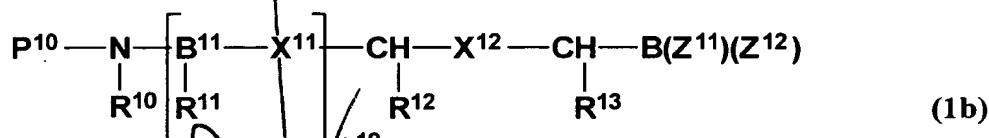
where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered
saturated, partially unsaturated or aromatic heterocycle, or

—chalcogen—alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A^{10} is 0, 1, or 2.

70. A method for reducing the rate of intracellular protein breakdown, comprising contacting cells in need of said reducing with an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

15 P¹⁰ is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

X^{11} , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B^{11} is N, then X^{11} is $-C(O)-NH-$;

X^{12} is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14

ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

5 R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

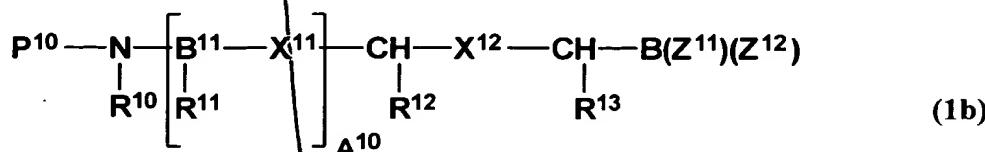
10 R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or -chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

15 Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and Z¹² together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

20 A¹⁰ is 0, 1, or 2.

71. A method for reducing the rate of degradation of p53 protein in a cell, comprising administering to a cell in need of said reducing an effective amount of a proteasome inhibitor of the formula:



25 or a pharmaceutically acceptable salt thereof;

wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

X¹¹, at each occurrence, is independently one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}_2-\text{NH}-$,
 $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$, $-\text{CH}(\text{OH})-\text{CH}-\text{NH}_2$, $-\text{CH}=\text{CH}-$,
5 $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$, provided
that when B¹¹ is N, then X¹¹ is $-\text{C}(\text{O})-\text{NH}$;

X¹² is one of $-\text{C}(\text{O})-\text{NH}-$, $-\text{CH}(\text{OH})-\text{CH}_2-$, $-\text{CH}(\text{OH})-\text{CH}(\text{OH})-$,
 $-\text{C}(\text{O})-\text{CH}_2-$, $-\text{SO}_2-\text{NH}-$, $-\text{SO}_2-\text{CH}_2-$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{C}(\text{O})-\text{NH}-$;

R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or
10 when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing
mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14
ring members, that can be optionally substituted by one or two of keto, hydroxy,
alkyl, aryl, aralkyl, alkoxy or aryloxy;

R¹¹, at each occurrence, is independently one of hydrogen, alkyl,
15 cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic
heterocycle or $-\text{CH}_2-\text{R}^{15}$, where the ring portion of any of said aryl, aralkyl,
alkaryl or heterocycle can be optionally substituted;

R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl,
20 aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or
 $-\text{CH}_2-\text{R}^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

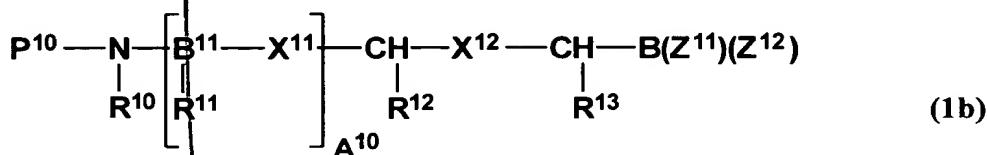
where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered
25 saturated, partially unsaturated or aromatic heterocycle, or
-chalcogen-alkyl, where the ring portion of any of said aryl,
alkaryl, alkaryl or heterocycle can be optionally substituted;

Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and
Z¹² together form a dihydroxy compound having at least two hydroxy groups
separated by at least two connecting atoms in a chain or ring, said chain or ring
comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can
30 be N, S, or O; and

A¹⁰ is 0, 1, or 2.

72. A method for inhibiting cyclin degradation in a cell, comprising contacting a cell in need of said reducing with an effective amount of a proteasome inhibitor of the formula:

5



or a pharmaceutically acceptable salt thereof;
wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

10 X¹¹, at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B¹¹ is N, then X¹¹ is $-C(O)-NH-$;

15 X¹² is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

20 R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

25 R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or

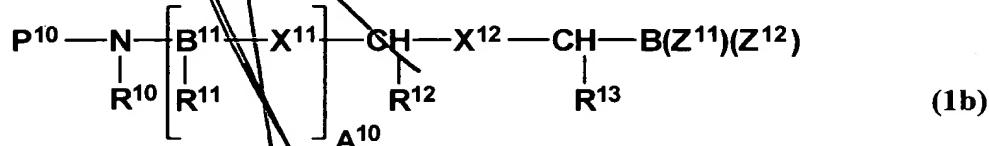
—CH₂—R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

5 where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or —chalcogen—alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

10 Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and Z¹² together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

15 A¹⁰ is 0, 1, or 2.

73. A method of preventing or treating an inflammatory condition in a patient in need thereof, said method comprising administering to said patient a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

20 P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

25 X¹¹, at each occurrence, is independently one of —C(O)—NH—, —CH₂—NH—, —CH(OH)—CH₂—, —CH(OH)—CH(OH)—, —CH(OH)—CH₂—NH—, —CH=CH—, —C(O)—CH₂—, —SO₂—NH—, —SO₂—CH₂— or —CH(OH)—CH₂—C(O)—NH—, provided that when B¹¹ is N, then X¹¹ is —C(O)—NH—;

X¹² is one of —C(O)—NH—, —CH(OH)—CH₂—, —CH(OH)—CH(OH)—, —C(O)—CH₂—, —SO₂—NH—, —SO₂—CH₂— or —CH(OH)—CH₂—C(O)—NH—;

R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

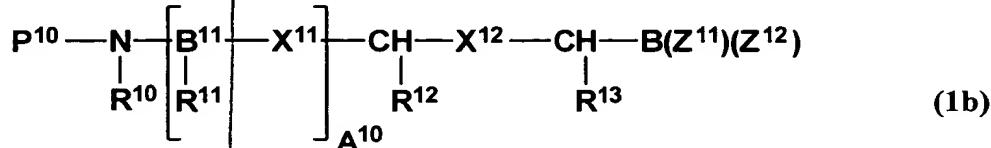
where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and Z¹² together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A¹⁰ is 0, 1, or 2.

74. The method of claim 73, wherein said patient has been diagnosed with, or is at risk of developing, a condition selected from the group consisting of tissue rejection, organ rejection, arthritis, an infection, dermatoses, inflammatory bowel disease, and an autoimmune disease.

75. A method for inhibiting antigen presentation in a cell comprising administering to a cell in need thereof an effective amount of a proteasome inhibitor of the formula:



5 or a pharmaceutically acceptable salt thereof;

wherein

P¹⁰ is hydrogen or an amino-group-protecting moiety;

B¹¹ is independently one of N or CH;

10 X¹¹, at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B¹¹ is N, then X¹¹ is $-C(O)-NH$;

X¹² is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

15 R¹⁰ is hydrogen or alkyl, or R¹⁰ forms together with the adjacent R¹¹, or when A¹⁰ is zero, forms together with the adjacent R¹², a nitrogen-containing mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

20 R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

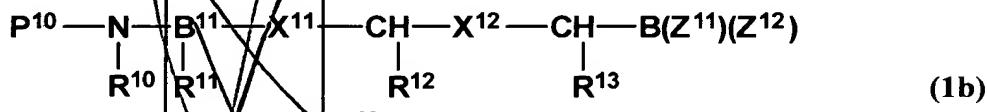
25 R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or -chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

5 Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and Z^{12} together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

10 A^{10} is 0, 1, or 2.

76. A method for inhibiting inducible NF- κ B dependent cell adhesion in an animal in need of said inhibiting, comprising administering to said animal an effective amount of a proteasome inhibitor of the formula:



15 or a pharmaceutically acceptable salt thereof;

wherein

P^{10} is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

20 X^{11} , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH_2-NH-$, $-CH=CH-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided that when B^{11} is N, then X^{11} is $-C(O)-NH-$;

25 X^{12} is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or when A^{10} is zero, forms together with the adjacent R^{11} , a nitrogen-containing

mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14 ring members, that can be optionally substituted by one or two of keto, hydroxy, alkyl, aryl, aralkyl, alkoxy or aryloxy;

R¹¹, at each occurrence, is independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

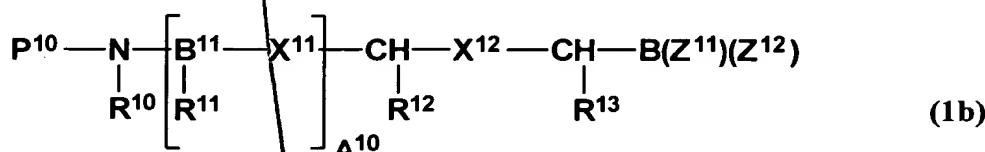
R¹² and R¹³ are each independently one of hydrogen, alkyl, cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or -CH₂-R¹⁵, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted,

where R¹⁵ is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle, or -chalcogen-alkyl, where the ring portion of any of said aryl, aralkyl, alkaryl or heterocycle can be optionally substituted;

Z¹¹ and Z¹² are independently alkyl, hydroxy, alkoxy, aryloxy, or Z¹¹ and Z¹² together form a dihydroxy compound having at least two hydroxy groups separated by at least two connecting atoms in a chain or ring, said chain or ring comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A¹⁰ is 0, 1, or 2.

77. A method for inhibiting HIV replication in an animal in need of said inhibiting, comprising administering to said animal an effective amount of a proteasome inhibitor of the formula:



or a pharmaceutically acceptable salt thereof;

wherein

P^{10} is hydrogen or an amino-group-protecting moiety;

B^{11} is independently one of N or CH;

X^{11} , at each occurrence, is independently one of $-C(O)-NH-$, $-CH_2-NH-$,
5 $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$, $-CH(OH)-CH-NH_2-$, $-CH=CH-$,
 $-C(O)-CH_2-$, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$, provided
that when B^{11} is N, then X^{11} is $-C(O)-NH$;

X^{12} is one of $-C(O)-NH-$, $-CH(OH)-CH_2-$, $-CH(OH)-CH(OH)-$,
-C(O)-CH₂-, $-SO_2-NH-$, $-SO_2-CH_2-$ or $-CH(OH)-CH_2-C(O)-NH-$;

10 R^{10} is hydrogen or alkyl, or R^{10} forms together with the adjacent R^{11} , or
when A^{10} is zero, forms together with the adjacent R^{12} , a nitrogen-containing
mono-, bi- or tri-cyclic, saturated or partially saturated ring system having 4-14
ring members, that can be optionally substituted by one or two of keto, hydroxy,
alkyl, aryl, aralkyl, alkoxy or aryloxy;

15 R^{11} , at each occurrence, is independently one of hydrogen, alkyl,
cycloalkyl, aryl, a 5-10 membered saturated, partially unsaturated or aromatic
heterocycle or $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl,
alkaryl or heterocycle can be optionally substituted;

20 R^{12} and R^{13} are each independently one of hydrogen, alkyl, cycloalkyl,
aryl, a 5-10 membered saturated, partially unsaturated or aromatic heterocycle or
 $-CH_2-R^{15}$, where the ring portion of any of said aryl, aralkyl, alkaryl or
heterocycle can be optionally substituted,

25 where R^{15} is aryl, aralkyl, alkaryl, cycloalkyl, a 5-10 membered
saturated, partially unsaturated or aromatic heterocycle, or
 $-chalcogen-alkyl$, where the ring portion of any of said aryl,
aralkyl, alkaryl or heterocycle can be optionally substituted;

Z^{11} and Z^{12} are independently alkyl, hydroxy, alkoxy, aryloxy, or Z^{11} and
 Z^{12} together form a dihydroxy compound having at least two hydroxy groups
separated by at least two connecting atoms in a chain or ring, said chain or ring

comprising carbon atoms, and optionally, a heteroatom or heteroatoms which can be N, S, or O; and

A¹⁰ is 0, 1, or 2.

78. The method of claims 67, 68, 69, 70, 71, 72, 73, 75, 76 or 77

5 wherein said proteosome inhibitor is one of:

N-(2-pyrazine)carbonyl-L-phenylalanine-L-leucine boronic acid,

N-(2-quinoline)sulfonyl-L-homophenylalanine-L-leucine boronic acid,

N-(3-pyridine)carbonyl-L-phenylalanine-L-leucine boronic acid,

N-(4-morpholine)carbonyl-L-phenylalanine-L-leucine boronic acid,

10 *N*-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,

N-(8-quinoline)sulfonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid,

N-(4-morpholine)carbonyl-(*O*-benzyl)-L-tyrosine-L-leucine boronic acid,

N-(4-morpholine)carbonyl-L-tyrosine-L-leucine boronic acid, or

15 *N*-(4-morpholine)carbonyl-[*O*-(2-pyridylmethyl)]-L-tyrosine-L-leucine boronic acid; or

isosteres, pharmaceutically acceptable salts or boronate esters thereof.

79. A method for reducing the rate of muscle protein degradation in a cell comprising contacting said cell with a compound of claim 58 or 61.

20 80. A method for reducing the activity of NF-κB in a cell comprising contacting said cell with a compound of claim 58 or 61.

81. A method for reducing the rate of intracellular protein breakdown comprising contacting cells with a compound of claim 58 or 61.

82. A method for reducing the rate of degradation of p53 protein in a cell comprising administering to said cell a compound of claim 58 or 61.

83. A method for inhibiting cyclin degradation in a cell comprising contacting said cell with a compound of claim 58 or 61.

5 84. A method of preventing or treating an inflammatory condition in a patient in need thereof, said method comprising administering to said patient a compound of claim 58 or 61.

10 85. The method of claim 84, wherein said patient has been diagnosed with, or is at risk of developing, a condition selected from the group consisting of tissue rejection, organ rejection, arthritis, an infection, dermatoses, inflammatory bowel disease, asthma, osteoporosis, osteoarthritis and an autoimmune disease

86. A method for inhibiting the growth of a cancer cell, comprising contacting said cell with a compound of claim 58 or 61.

87. A method for inhibiting antigen presentation in a cell comprising administering to said cell a compound of claim 58 or 61.

15 88. A method for inhibiting NF-κB dependent cell adhesion in an animal comprising administering to said animal a compound of claim 58 or 61.

89. A method for inhibiting HIV replication in an animal comprising administering to said animal a compound of claim 58 or 61.